Probiotics for preterm infants

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Probiotics

- Probiotics are a controversial issue
  - Responsible for the obesity epidemics
  - No more benefits than eating yoghurt
- Part of controversy is due to lack of precise definition

Definition

- Probiotics
  - Live microorganisms that when administered in adequate amounts confer a health benefit to the host
- Prebiotics
  - A substrate that is selectively utilized by host microorganisms conferring a health benefit
- Synbiotics
  - Dietary food supplements combining probiotics with prebiotics that support the chosen probiotics

Probiotics

- A micro-organism of human origin
- Non-pathogenic
- Resistant to destruction by technical processing & GIT secretions
- Able to colonise the GIT
- Capable of producing antimicrobial substances
- Modulating immune responses
- Influencing human metabolic activities

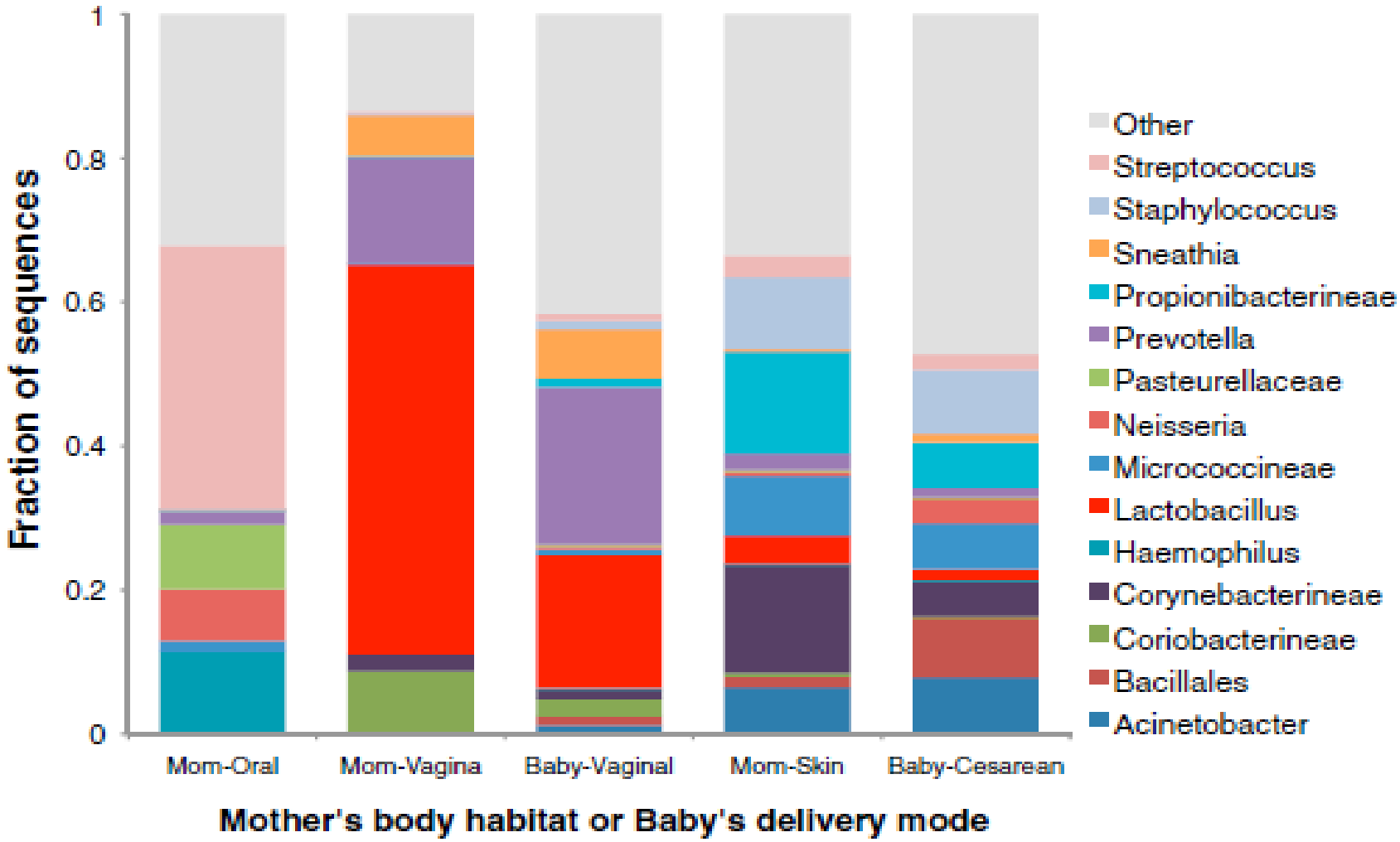
The human intestinal microbiome

At birth, the infant's gastrointestinal tract (GI tract) is essentially "sterile".

Colonization of the GI tract starts immediately after birth with the initiation of enteral feeding, and is well established within the first few days of life.

Intestinal flora varies widely from person to person. In adults, normal intestinal microflora consists of more than 100,000 billion bacterial cells comprising more than 400 different species.

Development of the infant microbiome



Dominguez-Bello et al, PNAS 2010.

The human intestinal microbiome

In formula-fed infants, coliforms, enterococci, and bacteroides predominantly colonize the intestinal tract. Bifidobacterium and Lactobacillus are present occasionally.

However, in breastfed infants, Bifidobacterium and Lactobacillus predominate with other enteric organisms being present less frequently.

The human intestinal microbiome

This pattern of bowel colonization is different in preterm infant in an intensive care setting.

Antibiotic use
infection control procedures
and delayed initiation of enteral feeding may influence the type and amount of micro-organisms colonizing the GI tract.

The human intestinal microbiome

The GI tract of ELBW infants are colonized by fewer than three bacterial species by the 10th day of life

Species of Bifidobacterium and Lactobacillus are found in the stool of less than 5% of patients studied within the 1st month of life

By day 30 of life, predominant organisms were enterobacteriaceae and coagulase-negative staphylococci, which are the most frequent pathogens responsible for nosocomial infection in the NICU.

Gewolb and colleagues. Arch Dis Child Fetal and Neonatal Ed. 1999

Probiotics for preterm infants

Probiotic bacteria are defined as live nonpathogenic bacteria species that normally reside in the GI tract of healthy term infants.

It has been postulated that introducing probiotics to preterm infants might be beneficial in order to avoid overgrowth of pathogenic organisms.

Probiotics supplementation has been proposed to enhance enteral feeding and prevent NEC and nosocomial infections in preterm infants.

Cochrane

Probiotics for preterm infants

The proposed beneficial effects of probiotic administration come from potentially competing with other organisms for binding sites and substrates in the bowel thereby:

- increasing the production of anti-inflammatory cytokines,
- decreasing the production of proinflammatory cytokines,
- reducing intestinal permeability,
- enhancing enteral nutrition.

Proposed benefits & mechanisms of action

Mechanism	Benefit
Reduction of mucosal permeability Increased mucus production Strengthening of intestinal tight junctions Inhibit of bacterial translocation	Maintenance of mucosal integrity
Modulation of microfluora growth &adherence Reduction of substances to aerobic bacteria Reduction of intraluminal PH Competitive exclusion of pathogenic bacteria from binding sites	Regulation of appropriate bacterial colonisation

Proposed benefits & mechanisms of action

Mechanism	Benefit
Increased fecal IgA production Enhanced mucosal IgA response Production of short chain fatty acids Increased blood leukocyte phagocytosis	Activation of general intestinal immune defenses
Increased T cell & macrophage production of cytokines Increased production of anti-inflammatory cytokines Decreased production of pro-inflammatory cytokines promotion of T lymphocyte helper cell cytokine profile	modulation of intestinal inflammation

Cochrane

Probiotics for preterm infants

A variety of probiotic agents may be available for study. *Lactobacillus* and *Bifidobacterium* species are available commercially in different forms and concentrations.

Does probiotic supplementation improve growth and feeding tolerance?

- Improved GIT motility
- Improved feeding tolerance
- Reduction in days of hospitalisation
- Improved weight gain
- Intestinal colonisation with probiotic organisms
- Favorably altered immune responses
- Decreased fungal colonisation in preterm

Effects of probiotic supplementation On

- Late onset sepsis
- Weight gain
- Neurodevelopmental outcome

In preterm infants is not supportive for routine use

Allergic diseases

Studies focused on

- Allergic diseases
  - Which result from dysfunction of immune regulation
- The Cochrane review reported an inconsistent effect of probiotics in atopic eczema
- Insufficient evidence to recommend for prevention of allergic disease or food hypersensitivity
- Most beneficial if commenced ante-natally and continued post-natally

Probiotics for term infants

- **Other reported benefits**
  - Enhanced vaccine effects
  - Increased feeding tolerance with less colic
  - Decreased antibiotic use

Caution

- **Caution** is still advised as rare adverse outcomes
  - Sepsis
  - Meningitis
  - Death
- With probiotic administration in immuno-compromised patients
- Neonates have an immature immune system

Probiotics for preterm infants

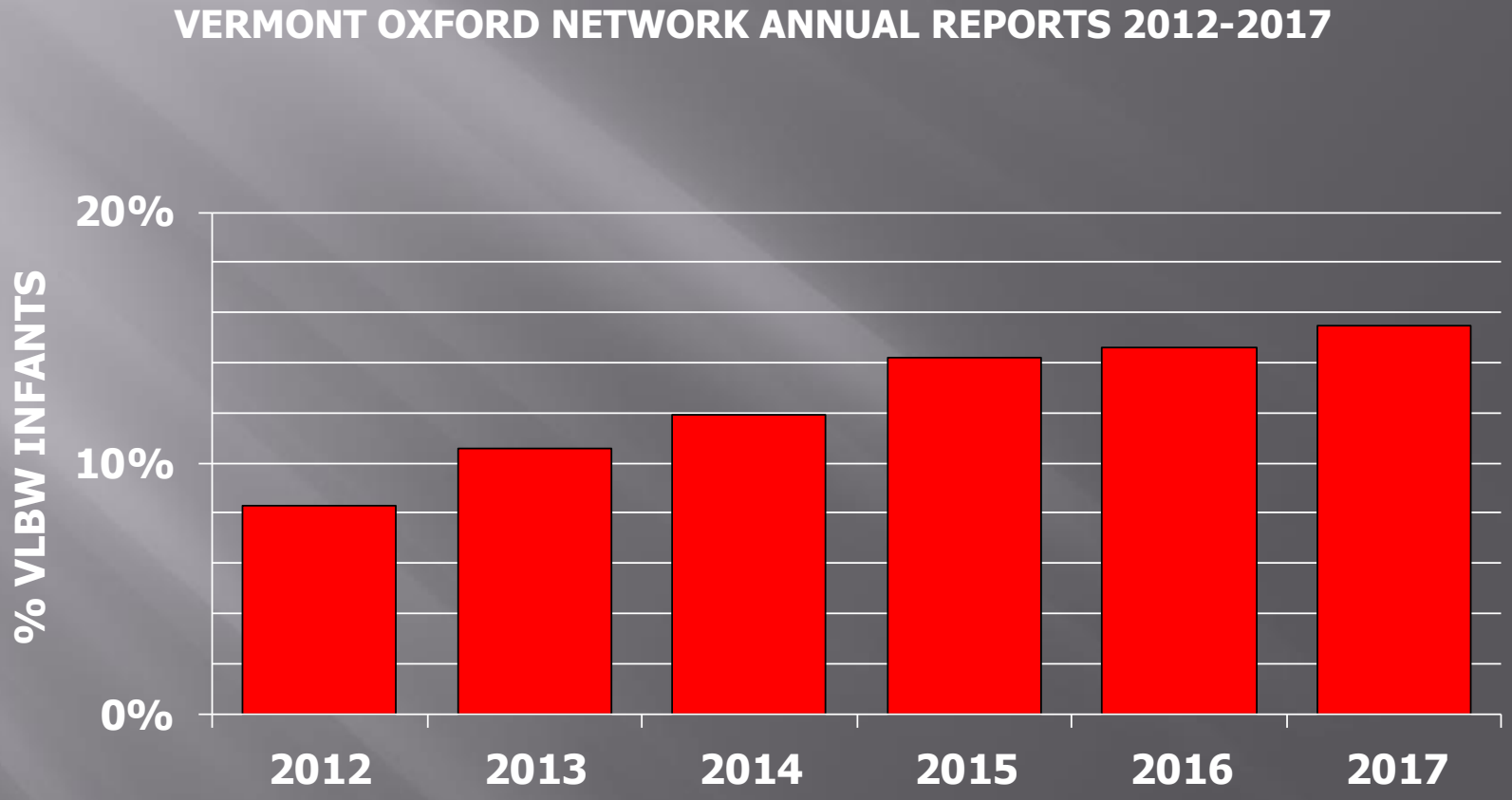
In the clinical trials, probiotic supplementation was not associated with any probiotic-related sepsis cases or any other adverse effects.

Probiotics for preterm infants

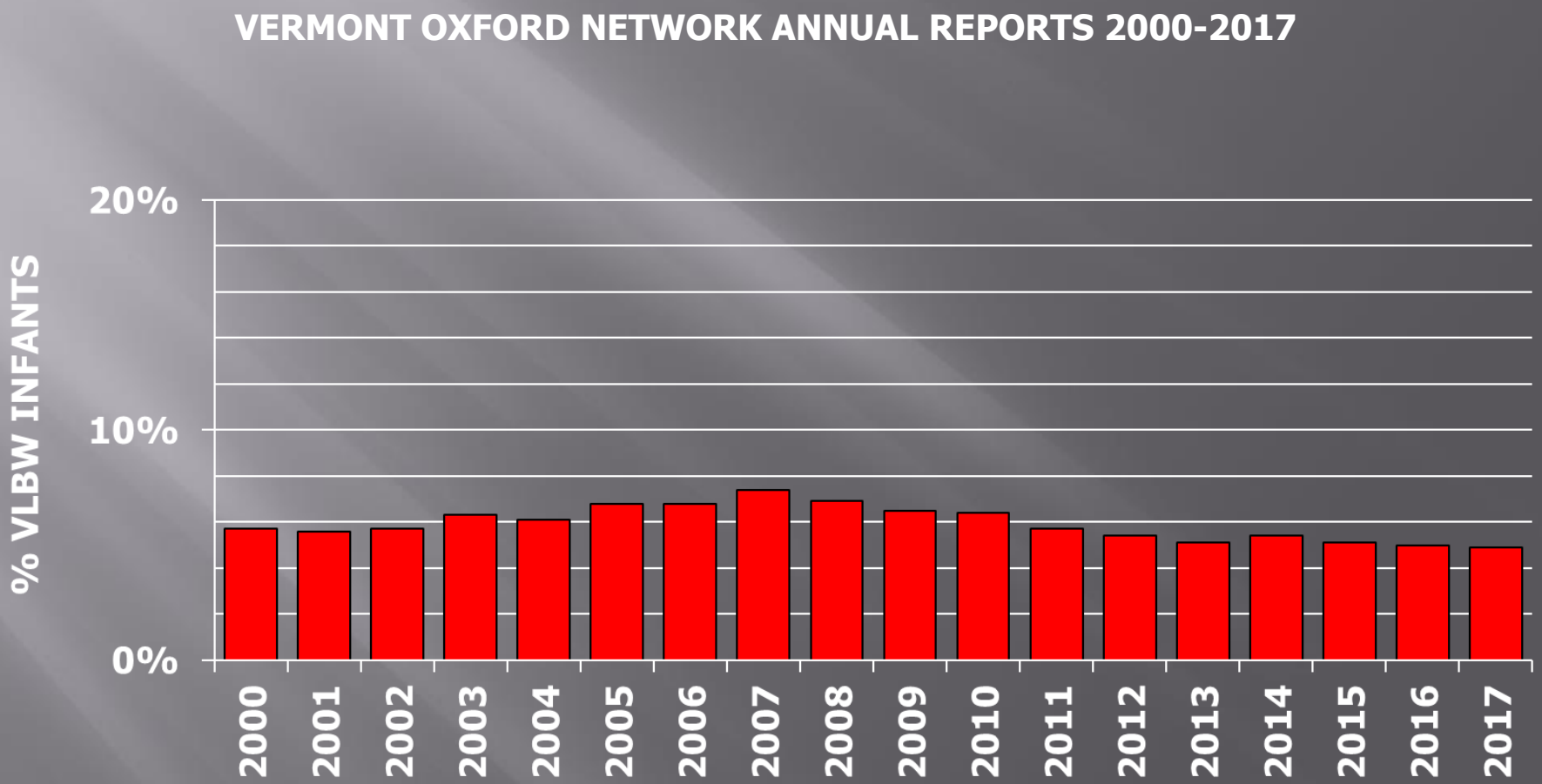
Current studies of probiotics:

- Multiple agents
- Multiple dosing strategies
- Few extremely low birth weight infants
- Few exclusively breast fed
- No product that has cleared regulatory hurdles

Probiotics in VLBW Infants



Necrotizing Enterocolitis in VLBW Infants



What to actually do?

What do we know about…

Benefits and Harms

- **Desirable Effects:** How substantial are the desirable anticipated effects?
- **Undesirable Effects:** How substantial are the undesirable anticipated effects?

Certainty of evidence: What is the overall certainty of the evidence of effects?

THANK YOU